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 NEWS 5 DEC 14 2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
 NEWS 6 DEC 14 CA/CAplus to be enhanced with updated IPC codes
         DEC 21 IPC search and display fields enhanced in CA/CAplus with the
 NEWS 7
                 IPC reform
         DEC 23
 NEWS 8
                 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                 USPAT2
 NEWS 9
         JAN 13
                 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS 10
         JAN 13
                 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                 INPADOC
 NEWS 11
                 Pre-1988 INPI data added to MARPAT
         JAN 17
 NEWS 12 JAN 17
                 IPC 8 in the WPI family of databases including WPIFV
 NEWS 13 JAN 30 Saved answer limit increased
 NEWS 14 JAN 31
                 Monthly current-awareness alert (SDI) frequency
                 added to TULSA
 NEWS EXPRESS JANUARY 03 CURRENT VERSION FOR WINDOWS IS V8.01,
              CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
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L3 20 L2

=> d ibib abs hitstr 1-20 it

L3 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:1315386 CAPLUS

DOCUMENT NUMBER:

144:45521

TITLE:

Dual-acting serotonin-norepinephrine reuptake

inhibitor (SNRI)-NMDA antagonists for the treatment of

genitourinary disorders

INVENTOR(S):

Thor, Karl Bruce

PATENT ASSIGNEE(S):

Dynogen Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 169 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	PATENT	NO.	KIND DATE				APPL	ICAT	ION I	DATE								
W	WO 2005117872					A2 20051215				WO 2	005-	US22	 897	20050603				
	W: AE, AG, AL,				AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
		CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	ΚP,	KR,	KZ,	
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	
		NG,	NI,	NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	
		SL,	SM,	SY,	ТJ,	TM,	TN,	TR,	TT,	ΤZ,	UA,	ŪG,	US,	UZ,	VC,	VN,	YU,	
		ZA,	ZM,	zw														
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	ΤZ,	UG,	ZM,	ZW,	AM,	
		ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IS,	ΙT,	LT,	LU,	MC,	NL,	PL,	PT,	
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	
		MR,	NE,	SN,	TD,	TG												
U	S 2005	A1		2005	1222	1	US 2	005-	1450	22		20	0050	603				
PRIORI	TY APE						US 2	004-	5769	99P	P 20040604							
								US 2004-607820P				P 20040907						
									1	US 2	004-	6401	05P]	P 20	0041	228	

AB Compns. and methods are discloses for treatment of genitourinary disorders (e.g., urge incontinence). The compns. may generally include a dual-acting SNRI-NMDA antagonist (e.g., bicifadine and/or milnacipran). Alternatively, the compns. may generally include an SNRI and an NMDA antagonist.

IT 186495-49-8 186495-55-6 186495-56-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

186495-49-8 CAPLUS

RN

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)

RN 186495-55-6 CAPLUS CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-, (β R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186495-56-7 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT Disease, animal

(Fowler's syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Glutamate antagonists

(NMDA antagonists; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Prostate gland, disease

(benign hyperplasia; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Hyperplasia

(benign prostatic; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems

(buccal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems

(capsules; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Pain

(chronic pelvic pain syndrome; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems

(controlled-release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Bladder, disease

Inflammation

(cystitis, interstitial (cell); dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Drug delivery systems

(delayed release; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for treatment of genitourinary disorders)

IT Urethra

(disease, urethritis; dual-acting serotonin-norepinephrine reuptake

```
inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΤT
     5-HT reuptake inhibitors
     Analgesics
     Anti-inflammatory agents
     Antitumor agents
     Bladder, disease
     Combination chemotherapy
     Drug delivery systems
     Human
     Neoplasm
     Urogenital system, disease
        (dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
        antagonists for treatment of genitourinary disorders)
IT
     Bladder, disease
        (hyperreflexia; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΤT
     Bladder, disease
        (incontinence; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
TΤ
     Drug delivery systems
        (inhalants; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT
     Drug delivery systems
        (intravesical; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT
     Drug delivery systems
        (mucosal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
        antagonists for treatment of genitourinary disorders)
ΙT
     Nervous system agents
        (noradrenaline reuptake inhibitors; dual-acting serotonin-
        norepinephrine reuptake inhibitor-NMDA antagonists for treatment of
        genitourinary disorders)
IT
     Drug delivery systems
        (oral; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
        antagonists for treatment of genitourinary disorders)
IT
        (orchidalgia; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Bladder, disease
        (overactive bladder, including overactive bladder with sphincter
        dysfunction; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
TΤ
     Disease, animal
        (pelvic hypersensitivity or sphincteric spasticity; dual-acting
        serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for
        treatment of genitourinary disorders)
TΤ
     Prostate gland, disease
        (prostadynia; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IT
     Inflammation
     Prostate gland, disease
        (prostatitis; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Drug delivery systems
        (pulsatile-release; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Drug delivery systems
        (rectal; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
        antagonists for treatment of genitourinary disorders)
ΙT
        (smooth muscle; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
        (smooth, urinary bladder; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Drug delivery systems
        (sublingual; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
IΤ
     Drug delivery systems
```

```
(sustained-release; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Drug delivery systems
        (tablets; dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
        antagonists for treatment of genitourinary disorders)
ΙT
     Drug delivery systems
        (transdermal; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Drug delivery systems
        (transurethral; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
        (urethra stricture disease; dual-acting serotonin-norepinephrine
        reuptake inhibitor-NMDA antagonists for treatment of genitourinary
        disorders)
     Inflammation
IT
        (urethritis; dual-acting serotonin-norepinephrine reuptake
        inhibitor-NMDA antagonists for treatment of genitourinary disorders)
ΙT
     Reproductive system
        (vulva, vulvodynia or vulvar vestibulitis; dual-acting
        serotonin-norepinephrine reuptake inhibitor-NMDA antagonists for
        treatment of genitourinary disorders)
ΙT
                14451-09-3, 5H-Dibenzo[a,d]cycloheptene-5-ethanamine
     21745-77-7, 9H-Xanthene-9-ethanamine
                                           21745-81-3, 9H-Thioxanthene-9-
     ethanamine 21745-82-4
                              21745-85-7
                                           28075-29-8
                                                       57226-64-9
                                           69096-48-6 71195-57-8
     63106-93-4
                 63940-51-2
                              66504-40-3
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                 105310-27-8
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     186496-71-9 200429-73-8
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     688738-12-7 871100-17-3
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     871100-21-9 871100-22-0
                                871100-23-1
                                              871331-21-4 871331-22-5
     871331-23-6 871331-24-7
                                871331-25-8
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (dual-acting serotonin-norepinephrine reuptake inhibitor-NMDA
       antagonists for treatment of genitourinary disorders)
    ANSWER 2 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                        2005:409336 CAPLUS
DOCUMENT NUMBER:
                        142:457117
TITLE:
                        Neuroprotective effects of gly-pro-glu following
                        intravenous infusion
                        Guan, Jian; Thomas, Gregory Brian; Batchelor, David
INVENTOR(S):
                        Charles; Gluckman, Peter David
PATENT ASSIGNEE(S):
                        Neuren Pharmaceuticals Ltd., N. Z.; Neuren
                        Pharmaceuticals Inc.
SOURCE:
                        PCT Int. Appl., 48 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
    PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
                                                                 DATE
                                          -----
    WO 2005042000
                        A1
                               20050512 WO 2004-US35165
                                                                 20041022
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRIORITY APPLN. INFO.:
                                            US 2003-513851P
                                                                    20031023
                                            US 2003-515397P
                                                                 Ρ
                                                                    20031028
                                            US 2004-553688P
                                                                 Ρ
```

AB Gly-Pro-Glu (GPE) is rapidly metabolized in vivo. We found that GPE infusion elicits potent and consistent neuroprotection in all brain regions examined, and in certain embodiments, the effects were greater than those of a bolus injection followed by infusion ('loading dose/infusion'). GPE reduced apoptosis in the hippocampus and inhibited microglial proliferation and prevented the injury-induced loss of astrocytes and improved long-term somatofunction. GPE after infusion showed a broad ED range (0.3-30mg/kg/h) and had a surprisingly extended window of treatment efficacy, permitting its use from 1 to at least as late as 24 h after neural injury. We also found that neuroprotective effects of acute GPE administration were prolonged and therefore capable of being used effectively to treat a variety of neurodegenerative conditions, even when administered after a neural injury. Thus, GPE can be an effective neuroprotective agent used either alone or co-administered along with other neuroprotective agents, antiinflammatory agents or peptidase or protease inhibitors. Compns. of GPE and protease and/or peptidase inhibitors are provided.

ΙT 186495-99-8, NPS 1506

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuroprotective effects of gly-pro-glu following i.v. infusion)

RN 186495-99-8 CAPLUS

CN

ΙT

Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)

HCl

ΙT Bone morphogenetic proteins RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(2; neuroprotective effects of gly-pro-glu following i.v. infusion) AIDS (disease)

(AIDS dementia complex; neuroprotective effects of gly-pro-glu following i.v. infusion)

ΙT Mental and behavioral disorders

> (AIDS dementia; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Brain, disease

Prion diseases

(Creutzfeldt-Jakob; neuroprotective effects of gly-pro-glu following i.v. infusion)

IT Growth factors, animal

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Glial activating factor; neuroprotective effects of gly-pro-glu following i.v. infusion)

```
Gene, animal
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (HSTF1; neuroprotective effects of gly-pro-glu following i.v. infusion)
ΙT
     Nervous system, disease
        (Huntington's chorea; neuroprotective effects of gly-pro-glu following
        i.v. infusion)
     Insulin-like growth factor-binding proteins
TΤ
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (IGFBP-3; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (LPAM-1 (lymphocyte Peyer's patch adhesion mol. 1); neuroprotective
        effects of gly-pro-glu following i.v. infusion)
ΙT
     Antibodies and Immunoglobulins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (MAdCAM-1; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IT
     Brain, disease
        (Schilder's disease; neuroprotective effects of gly-pro-glu following
        i.v. infusion)
IT
     Nervous system, disease
        (amyotrophic lateral sclerosis; neuroprotective effects of gly-pro-glu
        following i.v. infusion)
ΙT
        (cerebral cortex; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Ischemia
        (cerebral; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IΤ
     Encephalomyelitis
        (chronic relapsing; neuroprotective effects of gly-pro-glu following
        i.v. infusion)
IT
     Surgery
        (coronary artery bypass; neuroprotective effects of gly-pro-glu
        following i.v. infusion)
ΙT
        (coronary, bypass surgery; neuroprotective effects of gly-pro-glu
        following i.v. infusion)
ΙT
        (corpus striatum; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IT
     Radiation
        (damage; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IT
     Nerve, disease
        (death; neuroprotective effects of gly-pro-glu following i.v. infusion)
IT
     Nerve, disease
     Nervous system, disease
        (degeneration; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Central nervous system, disease
        (demyelination; neuroprotective effects of gly-pro-glu following i.v.
IT
     Brain
        (dentate gyrus; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Mental and behavioral disorders
        (depression; neuroprotective effects of gly-pro-glu following i.v.
IT
     Surgery
        (elective; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Neurotrophic factors
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
```

ΙT

```
(glial-derived; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IT
     Injury
        (head and neck; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IT
        (hippocampus, sector CA1; neuroprotective effects of gly-pro-glu
        following i.v. infusion)
ΙT
     Brain
        (hippocampus, sector CA2; neuroprotective effects of gly-pro-glu
        following i.v. infusion)
TΤ
     Brain
        (hippocampus, sector CA3; neuroprotective effects of qly-pro-qlu
        following i.v. infusion)
ΙT
     Brain
        (hippocampus, sector CA4; neuroprotective effects of gly-pro-glu
        following i.v. infusion)
ΙT
     Drug delivery systems
        (infusions, i.v.; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Head and Neck, disease
     Nerve, disease
     Reperfusion
        (injury; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Gene, animal
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (int-2; neuroprotective effects of gly-pro-glu following i.v. infusion)
ΙT
     Brain, disease
     Nerve, disease
        (ischemia; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Brain, disease
        (leukoencephalopathy; neuroprotective effects of gly-pro-glu following
        i.v. infusion)
IT
     Neuroglia
        (microglia; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Inflammation
     Spinal cord, disease
        (myelitis; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Inflammation
     Nerve, disease
        (neuritis; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IT
     Nerve, neoplasm
        (neuroblastoma; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
IΤ
     Cell death
        (neuron; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Injury
     Ischemia
        (neuronal; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
ΙT
     Alzheimer's disease
     Anti-Alzheimer's agents
     Anti-inflammatory agents
     Anticonvulsants
     Antidepressants
     Antiparkinsonian agents
     Antipsychotics
     Asphyxia
     Astrocyte
     Down's syndrome
     Encephalitis
     Encephalomyelitis
```

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Epilepsy
Hypoxia
Inflammation
Leukemia
Meningitis
Multiple sclerosis
Parkinson's disease
Schizophrenia
Spinal muscular atrophy
   (neuroprotective effects of gly-pro-glu following i.v. infusion)
Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
   (neuroprotective effects of gly-pro-glu following i.v. infusion)
Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (neuroprotective effects of gly-pro-glu following i.v. infusion)
Proliferating cell nuclear antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (neuroprotective effects of gly-pro-glu following i.v. infusion)
Insulin-like growth factor-binding proteins
Interleukins
Neurotrophic factors
Tumor necrosis factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (neuroprotective effects of gly-pro-glu following i.v. infusion)
Cytoprotective agents
   (neuroprotective; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Nervous system, disease
   (optic neuromyelitis; neuroprotective effects of gly-pro-glu following
   i.v. infusion)
Nerve, disease
   (peripheral neuropathy; neuroprotective effects of gly-pro-glu
   following i.v. infusion)
Brain, disease
   (progressive multifocal leukoencephalopathy; neuroprotective effects of
   gly-pro-glu following i.v. infusion)
Paralysis
   (pseudobulbar; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Injury
   (reperfusion; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (somatotropin-binding; neuroprotective effects of gly-pro-glu following
   i.v. infusion)
Brain, disease
Brain, disease
   (stroke; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Brain, disease
   (trauma; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (a; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (\alpha 4\beta 1; neuroprotective effects of gly-pro-glu following i.v.
   infusion)
Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (\beta 1-; neuroprotective effects of gly-pro-glu following i.v.
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infusion)
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     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (β; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
TΤ
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (γ; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
     9001-92-7, Proteinase
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (hibitors; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
TT
     9015-82-1, Peptidyldipeptidase
                                      9031-94-1, Aminopeptidase
                                                                  9031-98-5,
                      9031-99-6, Dipeptidase
     Carboxypeptidase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitor; neuroprotective effects of gly-pro-glu following i.v.
        infusion)
     56-40-6, Glycine, biological studies
                                            56-86-0, L-Glutamic acid,
TΤ
     biological studies 147-85-3, Proline, biological studies
                                                                  704-15-4
     RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL
     (Biological study)
        (neuroprotective effects of gly-pro-glu following i.v. infusion)
IT
     37205-61-1, Proteinase inhibitor 37259-58-8, Serine protease
     37353-41-6, Cysteine protease 123584-45-2, Fibroblast growth factor 4
     130939-41-2, Fibroblast growth factor 6
                                               145266-99-5, Metalloproteinase
                 148348-14-5, Fibroblast growth factor 3 169592-56-7,
     inhibitor
     Caspase-3
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (neuroprotective effects of gly-pro-glu following i.v. infusion)
     32302-76-4
ΤТ
     RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (neuroprotective effects of gly-pro-glu following i.v. infusion)
TΤ
     492-27-3, Kynurenic acid 533-45-9, Clomethiazole 9002-72-6, Growth
               9061-61-4, Nerve growth factor
                                               9087-70-1, Aprotinin
     14611-51-9, Selegiline 26305-03-3, Pepstatin A
                                                        30827-99-7, AEBSF
     50913-82-1, ORG 2766
                            55123-66-5, Leupeptin
                                                    58970-76-6, Bestatin
     66701-25-5
                  67763-96-6, IGF-1 67763-97-7, IGF-II
                                                           77086-22-7, MK-801
     80714-61-0, Semax
                        104987-11-3, Tacrolimus
                                                  106096-92-8, Acidic
     fibroblast growth factor 106096-93-9, Basic fibroblast growth factor
     106956-32-5, Oncostatin M 114949-22-3, Activin
                                                        118876-58-7, NBQX
     130939-66-1, Neurotrophin 3
                                 143375-33-1, Neurotrophin 4
                                                               148348-15-6,
     Keratinocyte growth factors
                                 161832-65-1, LY 300164
                                                            161832-71-9, LY
     303070
              171758-70-6, Keratinocyte growth factor 2 186495-99-8,
     NPS 1506
                                                           524706-48-7, GV
                204719-95-9, Fibroblast growth factor 16
     1505260
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (neuroprotective effects of gly-pro-glu following i.v. infusion)
REFERENCE COUNT:
                         2
                               THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 3 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
L3
ACCESSION NUMBER:
                         2004:1059129 CAPLUS
DOCUMENT NUMBER:
                         142:32998
TITLE:
                         Compositions of a cyclooxygenase-2 selective inhibitor
                         and a cannabinoid agent for the treatment of central
                         nervous system damage
INVENTOR(S):
                         Stephenson, Diane T.; Taylor, Duncan P.
PATENT ASSIGNEE(S):
                         Pharmacia Corporation, USA
SOURCE:
                         PCT Int. Appl., 177 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
                         1
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PATENT INFORMATION:

PAT	ENT	NO.			KIN	D	DATE			APPL	ICAT		DATE				
WO :	 2004	1056	99		A2	_	 2004	1209	,	WO 2	 004-		20040526				
WO :	2004	004105699			A3		20051215										
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DŽ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
		TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,
		SN,	TD,	TG													
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PRIORITY APPLN. INFO.:

US 2003-473820P P 20030528

OTHER SOURCE(S):

MARPAT 142:32998

The present invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a cannabinoid agent in combination with a cyclooxygenase-2 selective inhibitor.

IT **186495-49-8**, Delucemine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)

IT Ischemia

(central nervous system; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Combination chemotherapy

Drug interactions

Ischemia

(compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Cannabinoids

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Central nervous system, disease

(ischemia; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Cytoprotective agents

(neuroprotective; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT Brain, disease

(stroke; compns. of a selective cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

IT 52-52-8, 1-Aminocyclopentanecarboxylic acid 56-40-6, Glycine, biological studies 83-98-7, OrPhenadrine 521-35-7, Cannabinol 726-99-8, Fluorofelbamate 1972-08-3, Dronabinol 7541-16-4 13956-29-1,

```
25451-15-4, Felbamate 35377-89-0, 1-Methoxy-endo-4-hydroxy-
     Cannabidiol
     9-oxabicyclo[3.3.1]nonane 38964-50-0
                                            53847-30-6, 2-Arachidonylglycerol
                           68134-81-6, Gacyclidine
                                                     71125-38-7, Meloxicam
     57982-78-2, Budipine
                               76163-87-6
                                           76163-88-7
     76163-84-3
                  76163-85-4
                                                         80286-75-5
     83002-04-4
                  92623-85-3, Milnacipran
                                            93438-65-4, Conantokin G
     96206-92-7, 2-Methyl-6-(phenylethynyl)pyridine
                                                      97240-79-4, Topiramate
     104454-71-9, Ipenoxazone 112924-45-5, Dexanabinol
                                                          117414-74-1,
                 117571-54-7
                                            120667-19-8
                              119784-07-5
                                                           123653-11-2,
     N-[2-(Cyclohexyloxy)-4-nitrophenyl]methanesulfonamide
                                                             124649-81-6
     128298-28-2, Remacemide
                               132472-31-2
                                            135025-56-8, 7-Chlorothiokynurenic
            136109-04-1
                          137159-92-3, Aptiganel
                                                  138047-56-0
                                                                 139051-78-8
     140835-14-9
                   142235-88-9
                                 143850-75-3
                                               144912-63-0
                                                             153322-05-5,
                  153504-81-5, Licostinel 155471-08-2 157182-49-5
     Lanicemine
     158328-22-4
                   160754-76-7
                                 161230-88-2
                                               161292-39-3
                                                             162011-90-7,
     Rofecoxib
                164178-33-0 166974-22-7
                                             168273-06-1
                                                           169590-41-4,
     Deracoxib
                169590-42-5, Celecoxib
                                        173186-99-7
                                                       176977-56-3,
     [6-Methoxy-2-(4-methoxyphenyl)benzo[b]furan-3-yl](4-cyanophenyl)methanone
     180200-68-4, 4-(4-Cyclohexyl-2-methyloxazol-5-yl)-2-
     fluorobenzenesulfonamide
                              181695-72-7, Valdecoxib
                                                          183232-66-8
     186495-49-8, Delucemine
                             192703-06-3
                                            193278-48-7
                                                         193356-17-1
     197077-52-4
                  197438-41-8
                                198470-84-7, Parecoxib
                                                          198710-92-8,
     Kaitocephalin
                     200430-63-3
                                   202409-33-4, Etoricoxib
                                                             202463-68-1
     202807-80-5
                  202914-18-9 212126-32-4, 2-(3,5-Difluorophenyl)-3-[4-
     (methylsulfonyl)phenyl]-2-cyclopenten-1-one
                                                 215123-80-1
                                                                 219810-59-0,
                 220991-20-8, Lumiracoxib
                                             220991-33-3
                                                           252374-41-7
     Neramexane
     253450-09-8, Besonprodil
                               256510-26-6
                                              266320-83-6
                                                            342047-49-8
     369640-27-7
                  803731-69-3
                               803731-70-6
                                               803731-71-7
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (compns. of a cyclooxygenase-2 selective inhibitor and a cannabinoid
        agent for treatment of central nervous system damage)
     329900-75-6, Cyclooxygenase 2
                                    329967-85-3, Cyclooxygenase-1
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (compns. of a selective cyclooxygenase-2 selective inhibitor and a
        cannabinoid agent for treatment of central nervous system damage)
     ANSWER 4 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2004:781548 CAPLUS
DOCUMENT NUMBER:
                         141:254405
TITLE:
                        Acute treatment with MgSO4 attenuates long-term
                        hippocampal tissue loss after brain trauma in the rat
AUTHOR(S):
                         Browne, Kevin D.; Leoni, Matthew J.; Iwata, Akira;
                         Chen, Xiao-Han; Smith, Douglas H.
CORPORATE SOURCE:
                         Department of Neurosurgery, University of
                         Pennsylvania, Philadelphia, PA, USA
                         Journal of Neuroscience Research (2004), 77(6),
SOURCE:
                         878-883
                        CODEN: JNREDK; ISSN: 0360-4012
PUBLISHER:
                        Wiley-Liss, Inc.
DOCUMENT TYPE:
                        Journal
LANGUAGE:
                        English
     Previous studies have shown that magnesium salts and the noncompetitive
     N-methyl-D-aspartate (NMDA) receptor antagonist, NPS 1506, attenuated
     short-term cognitive deficits and histopathol. changes associated with
     traumatic brain injury (TBI). We evaluated the long-term effects of both
     therapies after brain trauma. Young adult rats were subjected to
    parasagittal fluid-percussion brain injury and received either MgSO4 (125
    \mumol/400 g rat; n = 12) 15 min post-injury, NPS 1506 (1.15 mg/kg; n =
    12) 15 min and 4 h post-injury, or vehicle (n = 9) 15 min post-injury.
    Uninjured animals (sham) received vehicle (n = 10). Learning function in
    these animals was evaluated using a water maze paradigm 8 mo after injury
    or sham treatment, and the brains were examined for cortical and hippocampal
    tissue loss. Compared to sham animals, injured vehicle-treated animals
```

displayed a substantial learning dysfunction, indicated by an increased latency to find a hidden platform in the water maze (P < 0.001). No improvements in learning, however, were found for injured animals treated

with NPS 1506 or MgSO4. Injury induced >30% loss of tissue in the ipsilateral cortex in vehicle-treated animals that was not reduced in animals treated with either NPS 1506 or MgSO4. Treatment with MgSO4

IT

significantly reduced progressive tissue loss in the hippocampus (P < 0.001). These findings are the first to demonstrate long-term neuroprotection of hippocampal tissue by an acute treatment in a TBI model. These data also show that the previously reported broad efficacy of MgSO4 or NPS 1506 observed shortly after brain trauma could not be detected 8 mo post-injury.

IT 186495-99-8, NPS 1506

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

RN 186495-99-8 CAPLUS

CN

Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)

● HCl

IT Cognition

Learning disorders

(MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

IT Glutamate antagonists

(NMDA antagonists; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

IT Brain

(cortex; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

IT Brain

(hippocampus, atrophy; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

IT Cytoprotective agents

(neuroprotective; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

IT Brain, disease

(trauma; MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

1T 7487-88-9, Sulfuric acid magnesium salt (1:1), biological studies 186495-99-8, NPS 1506

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(MgSO4 attenuates long-term hippocampal tissue loss after brain trauma in rat)

REFERENCE COUNT:

THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:353140 CAPLUS

DOCUMENT NUMBER:

140:380634

TITLE:

SOURCE:

LANGUAGE:

Compositions of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for the treatment or $\,$

prevention of neuropathic pain

INVENTOR(S): Cheung, Raymond Y.

PATENT ASSIGNEE(S):

Pharmacia Corporation, USA
U.S. Pat. Appl. Publ., 51 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATE	KIND DATE				APPL	ICAT	ION I		DATE								
US 20	A1 A2		2004 2004			US 2											
WO 2004039371					A3	A3 20040617											
V	W: AE, AG, AL,		AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,		
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	GE,
		GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,
		LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,
		OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,	TM,
		TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW		
F	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
RITY A	INFO	. :	US 2002-282660								• • •						
R SOUR			MARPAT 140:380634														

PRIOR OTHER

AΒ The present invention provides compns. and methods to treat or prevent neuropathic pain in a subject using a combination of a COX-2 selective inhibitor and a NMDA receptor antagonist.

ΙT 186495-49-8, Delucemine

> RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) INDEX NAME)

IT Glutamate receptors

> RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (NMDA-binding; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

ΙT Pain

TΤ

(neuropathic; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

Nerve, disease IT

> (neuropathy, related pain, treatment of; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

ΙΤ Drug delivery systems

> (prodrugs; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain) 329900-75-6, COX-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (COX-2; compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

IT 52-52-8, 1-Aminocyclopentane-carboxylic acid 56-40-6, Glycine, biological studies 83-98-7, Orphenadrine 125-71-3, Dextromethorphan 254-04-6, 2H-1-Benzopyran 726-99-8, Fluorofelbamate 768-94-5, Amantadine 6740-88-1, Ketamine 19982-08-2, Memantine 25451-15-4, Felbamate 57982-78-2, Budipine 68134-81-6, Gacyclidine 70172-33-7 71125-38-7, Meloxicam 92623-85-3, Milnacipran 93438-65-4, Conantokin G 96206-92-7, 2-Methyl-6-(phenylethynyl)-pyridine 97240-79-4, Topiramate 104454-71-9, Ipenoxazone 112924-45-5, Dexanabinol 117414-74-1, 123653-11-2, {N-[2-(Cyclohexyloxy)-Midafotel 117571-54-7 120667-19-8 4-nitrophenyl]methanesulfonamide} 128298-28-2, Remacemide 132472-31-2 134234-12-1, Traxoprodil 135025-56-8, 7-Chlorothiokynurenic acid

139051-78-8 137159-92-3, Aptiganel 138047-56-0 136109-04-1 153322-05-5, Lanicemine 142235-88-9 143850-75-3 144912-63-0 153504-81-5, Licostinel 160754-76-7 161230-88-2 161292-39-3 169590-41-4, Deracoxib 162011-90-7, Rofecoxib 166974-22-7 169590-42-5, Celecoxib 170029-85-3 173186-99-7 180200-68-4, 4-(4-Cyclohexyl-2-methyloxazol-5-yl)-2-fluorobenzenesulfonamide 181695-72-7, Valdecoxib **186495-49-8**, Delucemine 193278-48-7 198470-84-7, Parecoxib 193356-17-1 197077-52-4 198710-92-8, Kaitocephalin 200430-63-3 202409-33-4, Etoricoxib 202807-80-5 212126-32-4, 2-(3,5-Difluorophenyl)-3-[4-202914-18-9 (methylsulfonyl)phenyl]-2-cyclopenten-1-o ne 219810-59-0, Neramexane 252374-41-7 253450-09-8, Besonprodil 266320-83-6, ABT 963 342047-49-8 369640-27-7 676451-52-8D, derivs. RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

L3 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:924889 CAPLUS

DOCUMENT NUMBER: 140:317215

TITLE: Synthesis and brain regional distribution of [11C]NPS

1506 in mice and rat: An N-methyl-D-aspartate (NMDA)

receptor antagonist

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Maeda, Minoru

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SOURCE: Biological & Pharmaceutical Bulletin (2003), 26(11),

1570-1573

CODEN: BPBLEO; ISSN: 0918-6158 Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal LANGUAGE: English

NPS 1506 [3-fluoro- γ -($\bar{3}$ -fluorophenyl)-N-methylbenzenepropamine] is representative of a non-psychotomimetic class of N-methyl-D-aspartate (NMDA) receptor antagonists. [11C]NPS 1506 was prepared at high radiochem. purity (>98%) with a specific activity of around 50 GBq/ μ mol at the end of synthesis by methylation of the desmethyl precursor with [11C]methyl iodide in the presence of NaH. Biodistribution of [11C]NPS 1506 in mice and rat demonstrated that uptake into the brain was rapid and occurred at high levels. [11C]NPS 1506 showed no appreciable specific binding in rodent brains under in vivo conditions, possibly because of both a large non-specific bound fraction and low in vitro binding affinity for NMDA receptors.

IT 677764-00-0P

PUBLISHER:

RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

RN 677764-00-0 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-(methyl-11C)-,
hydrochloride (9CI) (CA INDEX NAME)

HC1

ΤT

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)

HC1

IT Glutamate antagonists

(NMDA antagonists; NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT Blood-brain barrier

Brain

Isotope indicators

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT Glutamate receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (NMDA-binding; NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT 677764-00-0P

RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT **186495-99-8P**, NPS 1506

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT 542-92-7, Cyclopentadiene, reactions 170019-10-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

IT 677763-98-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(NMDA receptor antagonist [11C]NPS 1506 preparation and brain distribution in mice and rat)

REFERENCE COUNT:

THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:396671 CAPLUS

DOCUMENT NUMBER: 138:379256

TITLE: Cyclic prolylglycine composition and therapeutic uses

INVENTOR(S):
Tran, Loi

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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                                            WO 2002-US36639
                                                                   20021112
     WO 2003041655
                          Α2
                                20030522
    WO 2003041655
                         A3
                                20040910
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
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             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
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                          AA
                                20030522
                                            CA 2002-2466701
                                                                   20021112
     US 2003109531
                          Α1
                                20030612
                                            US 2002-292732
                                                                   20021112
PRIORITY APPLN. INFO.:
                                            NZ 2001-515432
                                                                A 20011113
                                            US 2002-405909P
                                                               P 20020826
                                            WO 2002-US36639
                                                                W 20021112
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AB The invention discloses compns. containing, and use of, cyclic prolylglycine, and analogs and mimetics thereof, as neuroprotective agents for the treatment and or prevention of neurol. disorders including but not limited to cerebral ischemia or cerebral infarction resulting from a range of phenomena, e.g. thromboembolic or hemorrhagic stroke, cerebral basospasms, hypoglycemia, cardiac arrest, status epilepticus, perinatal asphyxia, anoxia (e.g. from drowning), pulmonary surgery, and cerebral trauma, as well as the treatment and prevention of chronic neurodenenerative disorders, e.g. Alzheimer's disease, Parkinson's disease, and Huntington's disease, and use as anticonvulsants.

IT 186495-99-8, NPS 1506

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclic prolylglycine composition and therapeutic uses, and use with other agents)

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)

HCl

IT Bone morphogenetic proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(2; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT Glutamate receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (AMPA-binding, antagonists; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT CD antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD106, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT CD antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD11A, agents against; cyclic prolylglycine composition and therapeutic uses, and use with other agents)

IT CD antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

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(CD18, agents against; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
TT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (FHF-1; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (FHF-2; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (FHF-3; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
IT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (FHF-4; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
IΤ
     Nervous system, disease
        (Huntington's chorea; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
ΙT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ICAM (intercellular adhesion mol.), agents against; cyclic
        prolylglycine composition and therapeutic uses, and use with other agents)
TΤ
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (LPAM-1 (lymphocyte Peyer's patch adhesion mol. 1), agents against;
        cyclic prolylglycine composition and therapeutic uses, and use with other
        agents)
IT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Leu-CAM (leukocytic cell adhesion mol.), agents against; cyclic
        prolylglycine composition and therapeutic uses, and use with other agents)
IT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (MAdCAM-1 (mucosal addressin cell adhesion mol.-1), agents against;
        cyclic prolylglycine composition and therapeutic uses, and use with other
        agents)
ΙT
     Tumor necrosis factors
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (TNF-\alpha; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
ΙT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (VCAM-1 (vascular cell adhesion mol. 1), agents against; cyclic
        prolylglycine composition and therapeutic uses, and use with other agents)
ΙT
     Cerebrospinal fluid
        (artificial; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
ΙT
     Brain
        (cerebellum, neurons; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
ΙT
        (cerebral; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
     Interferons
IT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (consensus\chi; cyclic prolylglycine composition and therapeutic uses, and
        use with other agents)
ΙT
     Surgery
        (coronary artery bypass, neurol. injury from; cyclic prolylglycine
        composition and therapeutic uses, and use with other agents)
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IT
     Artery
        (coronary, bypass surgery, neurol. injury from; cyclic prolylglycine
        composition and therapeutic uses, and use with other agents)
IT
     Alzheimer's disease
     Anti-Alzheimer's agents
     Anti-inflammatory agents
     Antiparkinsonian agents
     Apoptosis
     Drug delivery systems
     Encephalomyelitis
     Glutamate antagonists
     Inflammation
     Multiple sclerosis
     Myelination
     Nerve
     Nerve, disease
     Nerve regeneration
     Nerve regeneration
     Nervous system agents
     Neuroglia
     Neuron
     Neurotoxicity
     Parkinson's disease
     Peptidomimetics
        (cyclic prolylglycine composition and therapeutic uses, and use with other
ΙT
     Ciliary neurotrophic factor
     Insulin-like growth factor-binding proteins
     Interleukins
     Leukemia inhibitory factor
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclic prolylglycine composition and therapeutic uses, and use with other
        agents)
IΤ
     Nerve, disease
        (death; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Nervous system, disease
        (degeneration; cyclic prolylglycine composition and therapeutic uses, and
        use with other agents)
ΙT
     Neurotrophic factors
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (glial-derived; cyclic prolylglycine composition and therapeutic uses, and
        use with other agents)
IΤ
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (hst/Kfgk gene product; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
ΙT
     Drug delivery systems
        (inhalants; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
ΙT
     Drug delivery systems
        (injections, i.m.; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
IT
     Drug delivery systems
        (injections, i.p.; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
ΙT
     Drug delivery systems
        (injections, i.v.; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
ΙT
     Drug delivery systems
        (injections, s.c.; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
ΙT
     Drug delivery systems
        (injections; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
ΙŢ
     Brain, disease
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Nerve, disease
   (injury; cyclic prolylglycine composition and therapeutic uses, and use with
   other agents)
Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (int-2; cyclic prolylglycine composition and therapeutic uses, and use with
   other agents)
Brain, disease
   (leucodystrophy; cyclic prolylglycine composition and therapeutic uses, and
   use with other agents)
Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (metabotropic, mGluR2; cyclic prolylqlycine composition and therapeutic
   uses, and use with other agents)
Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (metabotropic, mGluR3; cyclic prolylglycine composition and therapeutic
   uses, and use with other agents)
Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (monoclonal, MECA-367; cyclic prolylglycine composition and therapeutic
   uses, and use with other agents)
Axon
   (myelination; cyclic prolylglycine composition and therapeutic uses, and use
   with other agents)
Inflammation
Spinal cord, disease
   (myelitis, transverse; cyclic prolylglycine composition and therapeutic
   uses, and use with other agents)
Drug delivery systems
   (nasal; cyclic prolylglycine composition and therapeutic uses, and use with
   other agents)
Encephalitis
   (necrotizing hemorrhagic; cyclic prolylglycine composition and therapeutic
   uses, and use with other agents)
Central nervous system
   (neurogenesis; cyclic prolylglycine composition and therapeutic uses, and
   use with other agents)
Asphyxia
   (neurol. injury from; cyclic prolylglycine composition and therapeutic uses,
   and use with other agents)
Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
   (neurol. injury from; cyclic prolylglycine composition and therapeutic uses,
   and use with other agents)
Nervous system, disease
   (neuromyelitis optica; cyclic prolylglycine composition and therapeutic
   uses, and use with other agents)
Cell death
   (neuron; cyclic prolylglycine composition and therapeutic uses, and use with
   other agents)
Injury
   (neuronal; cyclic prolylglycine composition and therapeutic uses, and use
  with other agents)
Cytoprotective agents
   (neuroprotective; cyclic prolylglycine composition and therapeutic uses, and
  use with other agents)
   (nigrostriatum; cyclic prolylglycine composition and therapeutic uses, and
  use with other agents)
Inflammation
Nerve, disease
   (optic neuritis; cyclic prolylglycine composition and therapeutic uses, and
  use with other agents)
Drug delivery systems
   (oral; cyclic prolylglycine composition and therapeutic uses, and use with
  other agents)
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ΙT
     Brain
        (pons, central pontine myelinolysis; cyclic prolylglycine composition and
        therapeutic uses, and use with other agents)
ΙT
     Brain, disease
        (progressive multifocal leukoencephalopathy; cyclic prolylglycine
        composition and therapeutic uses, and use with other agents)
ΙT
     Drug delivery systems
        (rectal; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Nervous system, disease
        (sclerosis, diffuse cerebral sclerosis of Schilder; cyclic
        prolylglycine composition and therapeutic uses, and use with other agents)
ΙT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (somatotropin-binding; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
     Brain, disease
        (stroke, neurol. injury from; cyclic prolylglycine composition and
        therapeutic uses, and use with other agents)
ΙT
     Drug delivery systems
        (systemic; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
ΙT
     Brain, disease
        (trauma; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Brain
        (white matter, damage; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
TΤ
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (\chi; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (a; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (αL, agents against; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (α4, agents against; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (\alpha 4\beta 1, agents against; cyclic prolylglycine composition and
        therapeutic uses, and use with other agents)
     Transforming growth factors
ΙT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (β1-; cyclic prolylglycine composition and therapeutic uses, and use
        with other agents)
TΤ
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (β; cyclic prolylglycine composition and therapeutic uses, and use with
        other agents)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (β7, agents against; cyclic prolylglycine composition and therapeutic
        uses, and use with other agents)
ΙΤ
     492-27-3, Kynurenic acid
                                533-45-9, Clomethiazole
                                                           2578-57-6
     2578-57-6D, analogs and peptidomimetics
                                              9002-72-6, Growth hormone
     9061-61-4, Nerve growth factor 14611-51-9, Selegiline
                                                                50913-82-1, ORG
            67763-96-6, Insulin-like growth factor 1 67763-97-7, Insulin-like
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growth factor 2 77086-21-6, Dizocilpine
                                                77086-22-7, MK-801
     80714-61-0, Semax 104987-11-3, FK506
                                            106096-92-8, Acidic fibroblast
     growth factor
                   106096-93-9, Basic fibroblast growth factor 106956-32-5,
                    109836-81-9, L-threo-1-Phenyl-2-decanoylamino-3-morpholino-
     Oncostatin M
     1-propanol
                  114949-22-3, Activin 118876-58-7, NBQX 123584-45-2,
     Fibroblast growth factor 4 130939-41-2, Fibroblast growth factor 6
     130939-66-1, Neurotrophin 3 140698-57-3, Activity-dependent neurotrophic
              143375-33-1, Neurotrophin 4
                                          148348-14-5, Fibroblast growth
                148348-15-6, Fibroblast growth factor 7 153436-22-7, GV
     factor 3
              161832-65-1, LY300164
                                     161832-71-9, LY303070
     150526
                                                             171758-70-6,
     Fibroblast growth factor 10 186495-99-8, NPS 1506
                                                        204719-95-9,
     Fibroblast growth factor 16
                                  524706-48-7, GV 1505260
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclic prolylglycine composition and therapeutic uses, and use with other
     56-86-0, L-Glutamic acid, biological studies
     RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
     unclassified); BIOL (Biological study)
        (glutamate toxicity; cyclic prolylglycine composition and therapeutic uses,
        and use with other agents)
     ANSWER 8 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                        2003:376586 CAPLUS
DOCUMENT NUMBER:
                        138:379245
TITLE:
                        Cyclo(prolylglycine) and methods of use to treat
                        neural disorders
INVENTOR(S):
                        Guan, Jian; Gluckman, Peter David; Sieg, Frank
PATENT ASSIGNEE(S):
                        Neuronz Limited, N. Z.; Neuronz Biosciences, Inc.
SOURCE:
                        PCT Int. Appl., 40 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                       KIND DATE
                                         APPLICATION NO.
                                                                DATE
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    WO 2003039487
                        A2
                               20030515
                                         WO 2002-US36235
                                                                  20021112
    WO 2003039487
                        А3
                               20040115
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PRIORITY APPLN. INFO.:
                                           NZ 2001-515371
                                                              A 20011109
                                           NZ 2001-515432
                                                              A 20011113
                                           NZ 2001-515551
                                                              A 20011116
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AB Embodiments of pharmaceutical compns. comprising cyclo(Pro-Gly) (cPG) and methods for use in treating neural degeneration are provided. The cPG substantially prevents toxic neural degeneration and cell death and promotes neurite outgrowth in neurons, especially cerebellar neurons. neuroprotective and neuroregenerative effects of cPG are useful to treat behavioral neurol. deficits involving motor control pathways.

ΙT 186495-99-8, NPS 1506

IT

L3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclo(prolylglycine) for treatment of neural disorders, and use with other agents)

186495-99-8 CAPLUS

RN

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)

HCl

IT Bone morphogenetic proteins RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) TΤ Glutamate receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (AMPA-binding, antagonists; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) Growth factors, animal TΤ RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Androgen-induced growth factor; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) ΙT CD antigens RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD106; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) CD antigens TΤ RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD11A; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) ΙT CD antigens RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD18; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) ΙT Brain, disease Nervous system, disease (Devic's disease; cyclo(prolylglycine) for treatment of neural disorders) Proteins ΙT RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (FHF-1; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) IΤ Proteins RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (FHF-2; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) ΙT Proteins RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (FHF-3; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) ΙT Proteins RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (FHF-4; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) IT Growth factors, animal RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Glial-activating factor; cyclo(prolylglycine) for treatment of neural disorders, and use with other agents) IT Nervous system, disease

(Huntington's chorea; cyclo(prolylglycine) for treatment of neural

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TΤ
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ICAM (intercellular adhesion mol.); cyclo(prolylglycine) for treatment
        of neural disorders, and use with other agents)
IT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (LPAM-1 (lymphocyte Peyer's patch adhesion mol. 1);
        cyclo(prolylglycine) for treatment of neural disorders, and use with
        other agents)
IT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (Leu-CAM (leukocytic cell adhesion mol.); cyclo(prolylglycine) for
        treatment of neural disorders, and use with other agents)
ΙT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (MAdCAM-1 (mucosal addressin cell adhesion mol.-1);
        cyclo(prolylglycine) for treatment of neural disorders, and use with
        other agents)
     Nervous system, disease
TT
        (Machado-Joseph; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Neuron
        (Purkinje cell, 5-fluorouracil- or cytosine arabinoside-induced loss of
        Purkinje cells; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Tumor necrosis factors
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (TNF-\alpha; cyclo(prolylglycine)) for treatment of neural disorders,
        and use with other agents)
ΙT
     Cell adhesion molecules
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (VCAM-1 (vascular cell adhesion mol. 1); cyclo(prolylglycine) for
        treatment of neural disorders, and use with other agents)
ΙT
     Encephalomyelitis
        (acute or chronic; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Cerebrospinal fluid
        (artificial; cyclo(prolylglycine) for treatment of neural disorders)
ΙΤ
     Neurotrophic factors
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (brain-derived; cyclo(prolylglycine) for treatment of neural disorders,
        and use with other agents)
ΙT
     Mvelin
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (central pontine myelinolysis; cyclo(prolylglycine) for treatment of
        neural disorders)
ΙT
     Brain
        (cerebellum, cerebellar neuron; cyclo(prolylglycine) for treatment of
        neural disorders)
ΙT
     Brain
        (cerebellum, damage; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Brain, disease
        (cerebellum, degeneration; cyclo(prolylglycine) for treatment of neural
        disorders)
ТТ
     Brain
        (cerebellum, hemorrhage; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Brain
        (cerebellum, infarction; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Injury
        (cerebral; cyclo(prolylglycine) for treatment of neural disorders)
TΤ
        (coronary artery bypass; cyclo(prolylglycine) for treatment of neural
        disorders)
IT
     Artery
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disorders)

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(coronary, bypass surgery; cyclo(prolylglycine) for treatment of neural
        disorders)
IT
     Brain
        (corpus striatum; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
        (cortex; cyclo(prolylglycine) for treatment of neural disorders)
     Peptides, biological studies
ΙT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclic; cyclo(prolylglycine) for treatment of neural disorders)
IT
     Alzheimer's disease
     Anti-Alzheimer's agents
     Anti-ischemic agents
     Antiparkinsonian agents
     Apoptosis
     Asphyxia
     Drug delivery systems
     Hypoxia
     Ischemia
     Motor skill disorders
     Necrosis
     Nerve
     Nervous system, disease
     Nervous system agents
     Neurotoxicity
     Parkinson's disease
     Wernicke-Korsakoff syndrome
        (cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Toxins
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (cyclo(prolylqlycine) for treatment of neural disorders)
IT
     Anti-inflammatory agents
     Glutamate antagonists
        (cyclo(prolylglycine) for treatment of neural disorders, and use with
        other agents)
ΙT
     Ciliary neurotrophic factor
     Insulin-like growth factor-binding proteins
     Interleukins
     Leukemia inhibitory factor
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclo(prolylglycine) for treatment of neural disorders, and use with
        other agents)
ΙT
     Nerve, disease
        (degeneration; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
        (dentate gyrus; cyclo(prolylglycine) for treatment of neural disorders)
IT
     Nervous system, disease
        (diffuse cerebral sclerosis of Schilder; cyclo(prolylqlycine) for
        treatment of neural disorders)
IT
        (drug-induced cerebellar disorders; cyclo(prolylglycine) for treatment
        of neural disorders)
ΙT
     Endocrine system
        (endocrine cerebellar disorders; cyclo(prolylglycine) for treatment of
        neural disorders)
IΤ
     Neurotrophic factors
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (glial-derived; cyclo(prolylglycine) for treatment of neural disorders,
        and use with other agents)
ΙT
     Brain
        (hippocampus, CA4; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Brain
        (hippocampus, sector CA1; cyclo(prolylglycine) for treatment of neural
        disorders)
IT
     Brain
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(hippocampus, sector CA2; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Brain
        (hippocampus, sector CA3; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (hst/Kfgk gene product; cyclo(prolylglycine) for treatment of neural
        disorders, and use with other agents)
ΙT
     Drug delivery systems
        (inhalants; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Drug delivery systems
        (injections, i.m.; cyclo(prolylglycine) for treatment of neural
        disorders)
IT
     Drug delivery systems
        (injections, i.p.; cyclo(prolylglycine) for treatment of neural
        disorders)
ΤT
     Drug delivery systems
        (injections, i.v.; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Drug delivery systems
        (injections, s.c.; cyclo(prolylglycine) for treatment of neural
        disorders)
IT
     Drug delivery systems
        (injections; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Brain, disease
        (injury; cyclo(prolylglycine) for treatment of neural disorders)
TΨ
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (int-2; cyclo(prolylglycine) for treatment of neural disorders, and use
        with other agents)
     Metabolism
ΙT
        (metabolic cerebellar disorders; cyclo(prolylglycine) for treatment of
        neural disorders)
TΤ
     Antibodies and Immunoglobulins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (monoclonal, MECA-367; cyclo(prolylglycine) for treatment of neural
        disorders, and use with other agents)
ΤΤ
     Nervous system, disease
        (multiple system atrophy; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Inflammation
     Spinal cord, disease
        (myelitis, transverse; cyclo(prolylglycine) for treatment of neural
        disorders)
IT
     Drug delivery systems
        (nasal; cyclo(prolylglycine) for treatment of neural disorders)
TΤ
     Encephalitis
        (necrotizing hemorrhagic; cyclo(prolylglycine) for treatment of neural
        disorders)
IΤ
     Nerve
        (neural fasciculation; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Nervous system, disease
        (neuromyelitis optica; cyclo(prolylglycine) for treatment of neural
        disorders)
IΤ
     Cytoprotective agents
        (neuroprotective; cyclo(prolylglycine) for treatment of neural
        disorders)
     Inflammation
ΙT
     Nerve, disease
        (optic neuritis; cyclo(prolylglycine) for treatment of neural
        disorders)
ΙT
     Drug delivery systems
        (oral; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Axon
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TΤ
     Gelatins, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical composition including; cyclo(prolylglycine) for treatment of
        neural disorders)
ΙT
     Brain, disease
        (progressive multifocal leukoencephalopathy; cyclo(prolylglycine) for
        treatment of neural disorders)
ΙT
     Drug delivery systems
        (rectal; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Proteins
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (somatotropin-binding; cyclo(prolylglycine) for treatment of neural
        disorders, and use with other agents)
     Nervous system, disease
IT
        (spinocerebellar ataxia 1; cyclo(prolylglycine) for treatment of neural
        disorders)
TΤ
     Nervous system, disease
        (spinocerebellar ataxia 6; cyclo(prolylglycine) for treatment of neural
        disorders)
TT
     Nervous system, disease
        (spinocerebellar ataxia, 2; cyclo(prolylglycine) for treatment of
        neural disorders)
IΤ
     Nervous system, disease
        (spinocerebellar ataxia, 4; cyclo(prolylglycine) for treatment of
        neural disorders)
ΙT
     Nervous system, disease
        (spinocerebellar ataxia, 5; cyclo(prolylglycine) for treatment of
        neural disorders)
TΤ
     Nervous system, disease
        (spinocerebellar ataxia, 7; cyclo(prolylglycine) for treatment of
        neural disorders)
ΙT
     Nervous system, disease
        (spinocerebellar ataxia, dominantly or recessively inherited;
        cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Nervous system, disease
        (spinocerebellar ataxia, sporadic; cyclo(prolylglycine) for treatment
        of neural disorders)
ΙΤ
     Brain, disease
        (stroke; cyclo(prolylglycine) for treatment of neural disorders)
IT
     Brain, disease
        (trauma; cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (\chi and consensus; cyclo(prolylglycine) for treatment of neural
        disorders, and use with other agents)
ΙT
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (a; cyclo(prolylglycine) for treatment of neural disorders, and
        use with other agents)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (αL; cyclo(prolylglycine) for treatment of neural disorders, and
        use with other agents)
TΤ
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (\alpha 4; cyclo(prolylglycine)) for treatment of neural disorders, and
        use with other agents)
ΙT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (α4β1; cyclo(prolylglycine) for treatment of neural
        disorders, and use with other agents)
ΙT
    Transforming growth factors
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        ($1-; cyclo(prolylglycine) for treatment of neural disorders, and
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(outgrowth; cyclo(prolylglycine) for treatment of neural disorders)

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use with other agents)
IT
     Interferons
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (β; cyclo(prolylglycine) for treatment of neural disorders, and
        use with other agents)
IT
     Integrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (β7; cyclo(prolylglycine) for treatment of neural disorders, and
        use with other agents)
ΙT
     51-21-8, 5-Fluorouracil
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (5-fluorouracil-induced loss of Purkinje cells; cyclo(prolylglycine)
        for treatment of neural disorders)
     64-17-5, Ethanol, biological studies
IT
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (alc. cerebellar degeneration; cyclo(prolylglycine) for treatment of
        neural disorders)
TT
     56-40-6, Glycine, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding; cyclo(prolylglycine) for treatment of neural disorders, and
        use with other agents)
     3705-27-9
ΙT
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclo(prolylglycine) for treatment of neural disorders)
TΤ
     492-27-3, Kynurenic acid
                                533-45-9, Clomethiazole 9002-72-6, Growth
               9061-61-4, Nerve growth factor
                                               14611-51-9, Selegiline
     50913-82-1, ORG 2766
                            67763-96-6, IGF-1
                                                67763-97-7, IGF-2
              80714-61-0, Semax
                                  104987-11-3, FK506
                                                       106096-92-8, Acidic
     fibroblast growth factor
                                106096-93-9, Basic fibroblast growth factor
     106956-32-5, Oncostatin M 109836-81-9, L-threo-1-Phenyl-2-decanoylamino-
     3-morpholino-1-propanol 114949-22-3, Activin
                                                     118876-58-7, NBQX
     123584-45-2, Fibroblast growth factor 4
                                              130939-41-2, Fibroblast growth
                130939-66-1, Neurotrophin 3 140698-57-3, Activity-dependent
     neurotrophic factor 143375-33-1, Neurotrophin 4
                                                        148348-14-5,
     Fibroblast growth factor 3
                                  148348-15-6, Fibroblast growth factor 7
     153436-22-7, GV 150526
                             161832-65-1, LY300164
                                                      161832-71-9, LY303070
     171758-70-6, Fibroblast growth factor 10 186495-99-8, NPS 1506
     204719-95-9, Fibroblast growth factor 16
                                                524706-48-7, GV 1505260
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cyclo(prolylglycine) for treatment of neural disorders, and use with
        other agents)
ΙΤ
     147-94-4, Cytosine arabinoside
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (cytosine arabinoside-induced loss of Purkinje cells;
        cyclo(prolylglycine) for treatment of neural disorders)
ΙT
     69-65-8, Mannitol
                        9004-54-0, Dextran, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical composition including; cyclo(prolylglycine) for treatment of
        neural disorders)
ΙT
     57-41-0, Phenytoin
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (phenytoin-induced cerebellar atrophy; cyclo(prolylglycine) for
        treatment of neural disorders)
     ANSWER 9 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2002:777693 CAPLUS
DOCUMENT NUMBER:
                         137:299911
TITLE:
                         Neuroprotectant formulations
INVENTOR(S):
                         Hesson, David P.; Frazer, Glenn D.; Ross, Douglas
PATENT ASSIGNEE(S):
                         Neuron Therapeutics, Inc., USA
SOURCE:
                         PCT Int. Appl., 28 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
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PATENT INFORMATION:

	PAT	CENT	NO.			KIN)	DATE				ICAT				DATE				
	WO	2002	0786 [°]	70		A1	_	2002	021010 WO 2002-US5885								20020228			
		W: AE, AG, AL,					ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,		
								DK,												
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,		
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,		
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	ΤZ,		
			UA,	UG,	UZ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	ΑZ,	BY,	KG,	ΚŻ,	MD,	RU,	ТJ,	TM	
		RW:	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	ΤZ,	UG,	ZM,	ZW,	AT,	ΒE,	CH,		
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								RO,												
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between the first and second catheters and c. maintaining the flow for a period of time adapted to perfuse an affected tissue.

ΙT 186495-99-8, NPS 1506

> RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (neuroprotectant formulations)

RN186495-99-8 CAPLUS

Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, CN hydrochloride (9CI) (CA INDEX NAME)

● HCl

Medical goods

Brain, disease

ΙT

ΙT

```
(catheters; neuroprotectant formulations)
ΙT
     Nervous system, disease
        (degeneration; neuroprotectant formulations)
ΙT
     Alzheimer's disease
     Anti-inflammatory agents
     Cerebrospinal fluid
     Drug delivery systems
     Human
     Multiple sclerosis
     Perfusion
        (neuroprotectant formulations)
ΙT
     Albumins, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (neuroprotectant formulations)
ΙT
     Cytoprotective agents
        (neuroprotective; neuroprotectant formulations)
IT
     Anti-inflammatory agents
        (nonsteroidal; neuroprotectant formulations)
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(stroke; neuroprotectant formulations)
ΙT
     Injury
        (trauma; neuroprotectant formulations)
ΙT
     169592-56-7, Caspase 3
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (inhibitor; neuroprotectant formulations)
ΙT
     50-81-7, Ascorbic acid, biological studies
                                                  51-55-8, Atropine, biological
               533-45-9, Clomethiazole
                                         987-78-0, Citicoline
                                                                2149-70-4,
                     2156-56-1, Ceresine
                                           6735-59-7, Pralidoxime
     Nitroarginine
                                                                    19982-08-2,
     Memantine
                 22059-21-8
                              22503-72-6
                                                        23210-56-2, Ifenprodil
                                           23052-81-5
                             55985-32-5, Nicardipine
     31409-32-2, MDL 27192
                                                       66085-59-4, Nimodipine
                        72784-47-5, ACPCE
     72784-43-1, ACPCM
                                             77086-21-6, Dizocilpine
     79055-68-8
                  88191-84-8, MDL 28170 107452-89-1, Ziconotide
     110347-85-8, Selfotel
                             111900-32-4
                                          112924-45-5, Sinnabidiol
     119431-25-3, Eliprodil
                            123931-04-4
                                           125546-04-5
                                                          128073-45-0
     128298-28-2, Remacemide 130931-65-6
                                             137160-11-3, Cerestat
     142852-51-5, TAK 147
                           144665-07-6, Lubeluzole
                                                      153504-81-5, Licostinel
     158798-83-5, AK 275
                           160399-35-9, AK 295
                                                 168021-79-2, NXY 059
     173952-44-8, SYM 2206
                             175615-45-9, LY 287041
                                                      185243-69-0, Etanercept
     186495-99-8, NPS 1506
                             223723-79-3, AEOL 10113
                                                       286475-30-7,
     AEOL 10150
                  466685-97-2
                                466685-98-3
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (neuroprotectant formulations)
REFERENCE COUNT:
                               THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L3
     ANSWER 10 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2000:814825 CAPLUS
DOCUMENT NUMBER:
                         135:55870
TITLE:
                         NPS 1506 Attenuates Cognitive Dysfunction and
                         Hippocampal Neuron Death Following Brain Trauma in the
AUTHOR(S):
                         Leoni, Matthew J.; Chen, Xiao-Han; Mueller, Alan L.;
                         Cheney, Jessica; McIntosh, Tracy K.; Smith, Douglas H.
                         Department of Neurosurgery, University of
CORPORATE SOURCE:
                         Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE:
                         Experimental Neurology (2000), 166(2), 442-449
                         CODEN: EXNEAC; ISSN: 0014-4886
PUBLISHER:
                         Academic Press
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     Although several noncompetitive N-methyl-D-aspartate (NMDA) receptor
     antagonists have been shown to be substantially efficacious in exptl.
     models of brain trauma, side effects associated with this class of compds.
     have impeded clin. application. Therefore, new noncompetitive NMDA
     receptor antagonists have been developed, including NPS 1506, that appear
     to be nontoxic but retain efficacy. In the present study, we evaluated
     the efficacy of NPS 1506 in a model of parasagittal fluid percussion brain
     trauma in the anesthetized rat. Administration of 1 mg/kg NPS 1506 at
    both 10 min and 4 h posttrauma induced no changes in brain temperature, mean
     arterial pressure, pulse, or arterial blood gasses. At 1 wk postinjury,
     animals treated with the same dosing regimen of NPS 1506 demonstrated a
     dramatic attenuation of memory dysfunction evaluated by a water maze task
     and had greatly reduced neuron death in the CA3 subfield of the
    hippocampus. However, NPS 1506 treatment did not significantly affect the
     extent of cortical tissue loss following injury. Since memory dysfunction
     and hippocampal damage are common and potentially related consequences of
    brain trauma in humans, our results suggest that NPS 1506 treatment may
    have clin. utility. (c) 2000 Academic Press.
ΙT
     186495-99-8
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death
        following brain trauma in rats)
```

RN

CN

186495-99-8 CAPLUS

hydrochloride (9CI) (CA INDEX NAME)

Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,

HC1

IT Cognition enhancers

(NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

IT Memory, biological

(disorder; NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

IT Brain, disease

(hippocampus, injury; NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

IT Cytoprotective agents

(neuroprotectants; NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

IT Brain, disease

(trauma; NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

IT 186495-99-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NPS 1506 attenuates cognitive dysfunction and hippocampal neuron death following brain trauma in rats)

REFERENCE COUNT:

57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2000:741905 CAPLUS

DOCUMENT NUMBER:

133:305610

TITLE:

Treatment of neurological disorders with nitric oxide

synthase inhibitors and excitatory amino receptor

modulators

INVENTOR(S):

O'Neill, Michael John

PATENT ASSIGNEE(S):

Eli Lilly and Company Limited, UK

SOURCE:

PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT	NO.			KIN	D	DATE			APPL	ICAT	DATE					
WO	2000	26		A2		20001019		,	WO 2	000-	GB12		20000406				
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		IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
		MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
		SK,	SL,	ТJ,	TM,	TR,	TT,	ΤZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,
		ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM								
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	ŪG,	ZW,	AT,	BE,	CH,	CY,	DE,
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
		CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG				
PRIORITY	APP	LN.	INFO	.:					1	GB 1	999-	1	A 19990409				
															_		

AB The present invention relates to a method of treating a neurol. disorder comprising administering to a patient an effective amount of a nitric oxide synthase inhibitor in combination with an effective amount of an excitatory amino receptor modulator. Combination of 2.5 mg/kg Mk-801, i.p., and 25

mg/kg ARL17477, i.p., had a synergistic degree of neuroprotection (78%) in cerebral ischemia induced in gerbils.

186495-99-8, NPS 1506

ΙT

RN

CN

IT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

186495-99-8 CAPLUS

Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-, hydrochloride (9CI) (CA INDEX NAME)

● HCl

IT Glutamate receptors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AMPA-binding, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators) Glutamate antagonists

(NMDA antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Nervous system

(disease; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Neurotransmitter antagonists

(excitatory amino acid; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Amino acids, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(excitatory, agonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Brain, disease

(ischemia, focal; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Brain, disease

(ischemia; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(kainate-binding, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(metabotropic, mGluR1, antagonists; treatment of neurol. disorders with nitric oxide synthase inhibitors and excitatory amino receptor modulators)

IT Glutamate receptors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

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(Uses)
        (metabotropic, mGluR2, agonists; treatment of neurol. disorders with
        nitric oxide synthase inhibitors and excitatory amino receptor
        modulators)
ΙT
     Glutamate receptors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (metabotropic, mGluR3, agonists; treatment of neurol. disorders with
        nitric oxide synthase inhibitors and excitatory amino receptor
        modulators)
     Glutamate receptors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (metabotropic, mGluR5, antagonists; treatment of neurol. disorders with
        nitric oxide synthase inhibitors and excitatory amino receptor
        modulators)
     Cytoprotective agents
ΙT
        (neuroprotectants; treatment of neurol. disorders with nitric oxide
        synthase inhibitors and excitatory amino receptor modulators)
ΙT
     125978-95-2, Nitric oxide synthase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; treatment of neurol. disorders with nitric oxide synthase
        inhibitors and excitatory amino receptor modulators)
     125-71-3, Dextromethorphan 125-73-5
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     7-Nitroindazole
                      19982-08-2, Memantine 23210-56-2, Ifenprodil
     25371-96-4, 1-(2-Trifluoromethylphenyl)imidazole
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                                       154164-30-4, Ym90k
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     191471-52-0, Ly379268
                             210245-80-0, Ym872 211566-75-5, Ly382884
     222529-89-7, LY 389795
                             301857-79-4, L-MIN 301857-80-7, Ramacemide
     301857-81-8, LY 377770
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (treatment of neurol. disorders with nitric oxide synthase inhibitors
        and excitatory amino receptor modulators)
     ANSWER 12 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:
                         2000:740404 CAPLUS
DOCUMENT NUMBER:
                         134:95398
TITLE:
                         NPS 1506, a moderate affinity uncompetitive NMDA
                         receptor antagonist: preclinical summary and clinical
                         experience
AUTHOR(S):
                         Mueller, A. L.; Artman, L. D.; Balandrin, M. F.;
                         Brady, E.; Chien, Y.; DelMar, E. G.; Kierstead, A.;
                         Marriott, T. B.; Moe, S. T.; Raszkiewicz, J. L.; Van
                         Wagenen, B.; Wells, D.
CORPORATE SOURCE:
                         NPS Pharmaceuticals, Inc., Salt Lake City, UT, USA
SOURCE:
                         Amino Acids (2000), 19(1), 177-179
                         CODEN: AACIE6; ISSN: 0939-4451
PUBLISHER:
                         Springer-Verlag Wien
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     NPS Pharmaceuticals, Inc. (NPS) has synthesized a series of open-channel
     blockers with varying potencies at the NMDA receptor. NPS 1506 is a
     moderate affinity antagonist that inhibits NMDA/qlycine-induced increases
     in cytosolic calcium in cultured rat cerebellar granule cells (IC50 =
     476nM) and displaces the binding of [3H]MK-801 to rat cortical membranes
     (IC50 = 664nM).
ΙT
     186495-99-8, NPS 1506
     RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
```

BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); PROC (Process); USES (Uses) (NPS 1506, a NMDA receptor antagonist, preclin. summary and clin. experience) $186495-99-8 \quad \text{CAPLUS}$ Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl-,

RN

CN

● HCl

IT Glutamate antagonists

(NMDA antagonists; NPS 1506 a NMDA receptor antagonist, preclin. summary and clin. experience)

IT Cytoprotective agents

(neuroprotectants; NPS 1506 a NMDA receptor antagonist, preclin. summary and clin. experience)

IT 186495-99-8, NPS 1506

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (NPS 1506, a NMDA receptor antagonist, preclin. summary and clin.

experience)

L3 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:381465 CAPLUS

hydrochloride (9CI) (CA INDEX NAME)

DOCUMENT NUMBER: 133:30571

TITLE: Preparation of aralkylamines active at

receptor-operated calcium channels as neuroprotectants INVENTOR(S): Mueller, Alan L.; Balandrin, Manuel F.; Vanwagenen,

Bradford C.; Delmar, Eric G.; Moe, Scott T.; Artman,

Linda D.; Barmore, Robert M.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: U.S., 133 pp., Cont.-in-part of WO 9511663.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.					KIN		DATE			APPLICATION NO.						DATE		
CA 2 WO 9	60719 21826 95216	80 12			A 20000606 AA 19950817 A2 19950817 A3 19950921					US 1 CA 1	995 - 994 <i>-</i>	4850 2182		19941026				
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CN 1 ES 2 EP 1	1483 10885 21561 1239	85 62 22			В Т3		2002	0616 0816		CN 1 ES 1 EP 2	994-	9320	57		19	99410 99410 99410	026	
PT 7	R: /4385 22239	3			${f T}$		2001	FR, 1031 1219		PT 1	994~	9320	57		19	99410	026	IE

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PRIORITY APPLN. INFO .:
                                             US 1994-194210
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                                             US 1994-288668
                                                                  B2 19940809
                                                                  A2 19941026
                                             WO 1994-US12293
                                                                  A2 19940811
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                                                                  A3 19941026
                                             EP 1994-932057
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                                                                  A2 19960607
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                                                                  A1 19970611
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                                                                  A1 19981104
                                                                  A1 20010402
                                             US 2001-825373
OTHER SOURCE(S):
                         MARPAT 133:30571
     Title compds., e.g., RCHR4CR1R5CR2R6R7 [R = (un)substituted Ph; R1, R5 = H,
     OH, (hydroxy)alkyl, alkoxy, acyloxy; R2,R6 = H or hydroxyalkyl; R1R2 =
     (CH2)n or (CH2)nNR3; R3 = H, alkyl, CH2CH2OH; R4 = (cyclo)alkyl, or
     (un) substituted Ph; R7 = N(R3)2; R7 = H when R1R2 = (CH2)nNR3; n = 1-6]
     were prepared Thus, (4-FC6H4)2CO was condensed with (EtO)2P(O)CH2CN and the
     product converted in 2 reduction steps to (4-FC6H4)2CHCH2CH2NH2. Data for
     biol. activity of title compds. were given.
ΙT
     186495-49-8P 186495-56-7P 186495-99-8P
     273409-53-3P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of aralkylamines active at receptor-operated calcium channels
```

as neuroprotectants) RN 186495-49-8 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)

RN 186495-56-7 CAPLUS

CN Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, α -dimethyl-, (α S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 186495-99-8 CAPLUS

CN Benzenepropanamine, 3-fluoro-γ-(3-fluorophenyl)-N-methyl-,
hydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 273409-53-3 CAPLUS

Benzenepropanamine, 3-fluoro- γ -(3-fluorophenyl)-N, β -dimethyl-(9CI) (CA INDEX NAME)

IT Ionophores

CN

(NMDA receptor complex; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT Glutamate receptors

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(NMDA-binding, ionophore complex; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

IT Nervous system

(degeneration, treatment; preparation of aralkylamines active at receptor-operated calcium channels as neuroprotectants)

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ΙT
     Cytoprotective agents
         (neuroprotectants; preparation of aralkylamines active at receptor-operated
        calcium channels as neuroprotectants)
ΙT
     Calcium channel
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
         (preparation of aralkylamines active at receptor-operated calcium channels
        as neuroprotectants)
ΙT
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                  28075-29-8P
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     273409-53-3P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of aralkylamines active at receptor-operated calcium channels
        as neuroprotectants)
ΙT
     62-23-7, p-Nitrobenzoic acid
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     Benzaldehyde, reactions
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                                                                 107-13-1.
     2-Propenenitrile, reactions
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     1,4-Diaminobutane
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             345-70-0, 3,3'-Difluorobenzophenone
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     5-Fluoroindole-3-acetic acid
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     3-Fluoro-2-methylbenzoyl chloride
                                          263355-05-1, 3-Fluoro-2-
     methylphenylmagnesium bromide
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of aralkylamines active at receptor-operated calcium channels
        as neuroprotectants)
TΤ
     455-67-4P
                 701-38-2P
                             4748-73-6P
                                           14209-32-6P
                                                         35513-93-0P
     38158-77-9P
                   51644-96-3P
                                 75762-57-1P
                                                83948-53-2P
                                                              98586-06-2P
     101187-29-5P
                    114459-62-0P
                                    122248-82-2P
                                                   122631-98-5P
                                                                   122632-01-3P
     122632-02-4P
                    128550-02-7P
                                    128550-03-8P
                                                   128550-05-0P
                                                                   128550-06-1P
     128550-07-2P
                    144923-52-4P
                                    147875-12-5P
                                                   147875-14-7P
                                                                   170018-87-8P
     170018-88-9P
                    170018-89-0P
                                    170018-90-3P
                                                   170018-92-5P
                                                                   170018-96-9P
     170018-97-0P
                    170019-07-5P
                                    170019-09-7P
                                                   170019-11-1P
                                                                   170019-14-4P
     170019-15-5P
                                    170019-17-7P
                    170019-16-6P
                                                   170019-18-8P
                                                                   170019-19-9P
     170019-20-2P
                    170019-21-3P
                                    170019-22-4P
                                                   170019-23-5P
                                                                   170019-24-6P
     170019-25-7P
                    186496-31-1P
                                    186496-32-2P
                                                   186496-33-3P
                                                                   186496-34-4P
     186496-35-5P
                                    186496-37-7P
                    186496-36-6P
                                                   186496-38-8P
                                                                   186496-39-9P
     186496-40-2P
                                    186496-42-4P
                    186496-41-3P
                                                   186496-44-6P
                                                                  186496-45-7P
     186496-46-8P
                    186496-48-0P
                                    186496-51-5P
                                                   186496-52-6P
                                                                  186496-53-7P
     273409-54-4P
                    273409-55-5P
                                    273409-56-6P
                                                   273409-57-7P
                                                                  273409-58-8P
     273409-62-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of aralkylamines active at receptor-operated calcium channels
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as neuroprotectants)